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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/903,520	07/11/2001	Avi Ashkenazi	10466/83	1093

35489 7590 12/23/2004

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EXAMINER	
ANDRES, JANET L	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 12/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/903,520	ASHKENAZI ET AL.	
	Examiner	Art Unit	
	Janet L. Andres	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 October 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *39-51* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *39-51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 30 August 2004 has been entered.

Claims 39-51 are pending and under examination in this office action. The text of those sections of Title 35, U.S. Code, not included in this action can be found in a prior office action.

Claim Rejections Maintained

The rejection of claims 39-51 under 35 U.S.C. 112, first paragraph, as lacking enablement is maintained for reasons of record in the office actions of 28 April 2004 and 26 November 2003.

Applicant has provided a declaration under 37 U.S.C. 1.132 form Dr. Sherman Fong and a section from Current Protocols in Immunology. Dr. Fong states that the MLR assay is a widely used proliferative assay of T-cell function. Dr. Fong describes the assay procedure and states that what is measured is the ability of a substance to induce dendritic cells to cause proliferation of T-cells that are activated in the MLR and thus it identifies agents that can boost the immune system. Dr. Fong points to IL-12 as such a stimulant and states that a PRO polypeptide that stimulates T-cell proliferation with an activity "at least 180% of control" would find practical utility as an immune stimulant. Current Protocols in Immunology provides protocols for performing and MLR. Applicant argues that Dr. Fong states that the MLR assay is useful for

detecting immunostimulatory activities of molecules like PRO335. Applicant argues that Current Protocols in Immunology also states that immune stimulants that can boost the response to a particular antigen can be identified. Applicant further argues that Steinman states that therapies that enhance immunity are needed and that Peterson shows the usefulness of one such agent, IL-12. Applicant concludes that the artisan would know, based on the results of the MLR assay, that PRO335 would be useful to boost the immune system, for example to treat cancer or HIV. Applicant argues that the skilled artisan would have an M.D. or Ph.D. and would know how to make and use such immunostimulants without undue experimentation.

Applicant's arguments and the declaration of Dr. Fong have been fully considered but have not been found to be persuasive. No "particular antigen" is identified in the specification; there is no guidance as to how PRO335 could be used to boost the response to any antigen. Current Protocols in Immunology states on p. 3.12.11 that the MLR "only detects dividing cells instead of measuring true effector T-cell function" and that it is "not clear which T cell function is measured in proliferative assays", and further that "the proliferative response should be used solely as a general indicators of T cell reactivity". Data obtained might variously reflect proliferation of CTL, lymphokine producing T cells, or non-activated bystander cells and will be severely affected by the function of non-T cells. Differences in responsiveness in a proliferative assay in part reflect differences in IL-2 production, according to Current Protocols in Immunology. As has been stated previously, the MLR measures the reactivity of one individual to another and is, as Current Protocols in Immunology states, highly variable. Current Protocols in Immunology in fact describes many variables that must be controlled for. In the instant application, no such controls, such as for maximum response or for the inherent variability of

individual responses, are provided. There is no indication of the statistical significance of the results. There are no autologous controls. No correlation is provided to any particular *in vivo* function; there is no guidance to indicate that PRO335 could be used to any therapeutic effect for the treatment of diseases such as cancer or HIV. The references cited by Applicant fail to provide compensatory guidance. Steinman and Thurner et al. address the utility of dendritic cells but not of a stimulatory MLR. Gubler describes the identification of the molecule IL-12 but uses the MLR merely to compare activities, not as the basis for describing a molecule as a therapeutically useful immunostimulant. The subsequent research of Peterson et al. was clearly required to suggest that the molecule could be used in this fashion. Thus, without further guidance correlating the observed stimulatory activity to a particular, useful property, it would require undue experimentation to use PRO335.

NO CLAIM IS ALLOWED.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Andres whose telephone number is 571-272-0867. The examiner can normally be reached on Monday, Tuesday, Thursday, Friday, 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on 571-272-0961. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Janet L. Andres, Ph.D.
21 December 2004

JANET ANDRES
PRIMARY EXAMINER